

Applicant: Aoki et al.
Serial No.: 09/845,514
Filed: April 30, 2001
Page 2 of 7

Remarks

As a preliminary matter, Applicant thanks and appreciates the courtesy shown by Patent Examiner Ford and Supervisory Patent Examiner Smith in granting Applicant's undersigned representative, Greg S. Hollrigel, Ph.D., a telephonic interview on March 12, 2003 to discuss the January 13, 2003 Office Action and the cited reference. A summary of the interview is presented herein. Applicant understands that the Examiner will consider the remarks made during the interview and the remarks presented herein in connection with the continued examination of this application.

Summary of Interview on March 12, 2003

On March 12, 2003, Applicant's undersigned representative, Greg S. Hollrigel, conducted an interview with Patent Examiner Ford and Supervisory Patent Examiner Smith to discuss the January 13, 2003 Office Action and the cited reference (U.S. Patent No. 5,562,907 to Arnon; the '907 patent).

As discussed, claims 1-9 and 17-29 are currently pending.

In the January 13, 2003 Office Action, claims 5, 21, and 29 have been objected to, in particular, claims 5, 21, and 29 have been rejected as being dependent upon a rejected base claim, but would be allowable if rewritten in independent from including all of the limitations of the base claim and any intervening claim. As the undersigned mentioned, claim 29 is an independent claim for a composition comprising a combination of botulinum neurotoxin A and botulinum neurotoxin E. Because claim 29 is already independent, claim 29 should be allowable in view of the remarks made in the January 13, 2003 Office Action.

The Office Action also indicates that claims 1-4, 6-9, 17-20, and 22-28 continue to be rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Arnon (U.S. Patent No. 5,562,907). In maintaining the rejection, the Office Action relies on page 19 of the priority document for the

Applicant: Aoki et al.
Serial No.: 09/845,514
Filed: April 30, 2001
Page 3 of 7

'907 patent (i.e., U.S. Application No. 08/062,110; the '110 application) for support of disclosure of a composition including a combination of two or more neurotoxins, and methods of using such compositions.

As the undersigned discussed with the Examiners, the main outstanding issue is whether the '907 patent is entitled to the filing date of the '110 application with respect to a composition containing a combination of botulinum toxins and methods of using such a composition. Examiner Ford agreed that this is the main outstanding issue.

Upon the undersigned's request, Examiner Ford indicated that support in the '110 application for a composition containing a combination of botulinum toxins is provided at page 19, lines 12-17 of the '110 application. The relevant passage from the '110 application, as identified by Examiner Ford, is set forth below:

The purified immunoglobulin was derived from pooled adult human plasma from persons immunized with pentavalent (ABCDE) botulinum toxoid, who were selected for their high titers of neutralizing antibody against botulinum neurotoxin types A, B, C, D, and E.

As the undersigned discussed with the Examiners, a botulinum toxoid is not a botulinum toxin, let alone a combination of botulinum toxins. A toxoid is an inactive derivative of a toxin. Typically, the activity of the toxin is destroyed by exposing the active toxins to chemicals, such as formaldehyde-type products.

In addition, the undersigned mentioned that in the '110 application, Arnon specifically and consistently discloses the use of a single botulinum toxin, and not a composition containing a combination of botulinum toxins. In particular, Arnon discloses the use of an antitoxin and a single botulinum toxin to provide therapeutic effects. For example, repeated reference to a single botulinum toxin may be found in the '110 application at least at page 1, lines 11-12 ("botulinum toxin"); page 15, lines 20-21 ("a toxin, such as a neurotoxin"), lines 26-27 ("the toxin"); page 16,

Applicant: Aoki et al.
Serial No.: 09/845,514
Filed: April 30, 2001
Page 4 of 7

line 17 ("patients treated with a toxin"), lines 33-34 ("any toxin"); page 17, line 7 ("botulinum toxin"); page 20, line 5 ("the treatment dose of botulinum toxin"); and elsewhere therein.

The disclosure of combinations of botulinum toxins that is present in the '907 patent is not present in the '110 application. For example, at column 11, line 50, the phrase "toxin(s)" was added to replace the previous use of the word "toxin" in the '110 application. In addition, the entire section from column 13, line 60 (starting with "Use of Combinations of Botulinum and Tetanus Toxins Together with Their Corresponding Antitoxins") to column 18, line 33 of the '907 patent is not present in the '110 application.

In addition, the undersigned discussed with the Examiners that if claims (i.e., claims 5, 21, and 29) directed to a composition containing botulinum toxin type A and botulinum toxin type E, and methods of using that composition were patentable over Arnon, it would appear that based on the disclosure of the '110 application, that claims for a composition comprising any combination of botulinum toxins (such as, A and B, A and C, A and D, B and C, etc.) should also be patentable over Arnon. Examiner Ford indicated that it would appear that the reasoning to support the patentability of claims 5, 21, and 29 should similarly apply to the other combinations of botulinum toxins recited in the other claims, but that further consideration would be needed before a decision is made.

Examiner Ford indicated that she would take into consideration the remarks made during the interview, and in this response to the January 13, 2003 Office Action in conducting further examination of this application.

Item 3 of the Office Action-Rejections Withdrawn

Applicant acknowledges that Applicant's previous response was sufficient to overcome the rejection of claims 1-9 and 17-29 under 35 U.S.C. § 102(e)/103 over Borodic.

Applicant: Aoki et al.
Serial No.: 09/845,514
Filed: April 30, 2001
Page 5 of 7

Items 4-5 of the Office Action-Rejection Under 35 U.S.C. § 102

The rejection of claims 1-4, 6-9, 17-20, and 22-28 under 35 U.S.C. § 102(e) as allegedly being anticipated by Arnon (U.S. Patent No. 5,562,907; the '907 patent) has been maintained.

Applicant respectfully traverses the rejection. As stated in Applicant's previous response, the '907 patent was filed on June 6, 1994 as a continuation-in-part of U.S. Application No. 08/062,110, which was filed on May 14, 1993. Applicant maintains that the '907 patent is not entitled to the May 14, 1993 priority date with respect to a composition or methods comprising a combination of botulinum toxins.

The effective filing date of the instant application is June 10, 1993. Accordingly, the instant application predates the disclosure of combinations of botulinum toxins disclosed in the '907 patent, and thus, the '907 patent is not prior art to the presently claimed invention.

As indicated above and discussed with the Examiners in the above-referenced interview, the '110 application discloses the use of a single type of botulinum toxin and an antitoxin for medical purposes. The '110 application does not disclose combinations of botulinum toxins. In addition, as indicated above, the '110 application's disclosure of using the botulinum toxoid to generate antibodies is not a disclosure of a composition containing a combination of botulinum toxins.

As discussed in Applicant's specification, a botulinum toxin is "a toxin that binds to presynaptic cholinergic nerve terminals and inhibits the exocytosis of acetylcholine" (page 1, lines 26-28). Botulinum toxoid, as identified in the '110 application, has been chemically inactivated and therefore, the toxoid cannot bind to presynaptic cholinergic nerve terminals and inhibit the exocytosis of acetylcholine. As evidence that it is well understood by persons of ordinary skill in the art that a toxoid is not a toxin, Applicant encloses herewith, as **Exhibit A**, the definition of "toxoid" as stated in The Concise Oxford Dictionary, Tenth Edition. As indicated therein, a toxoid is "a chemically modified toxin from a pathogenic micro-organism, which is **no longer toxic** but is still antigenic and can be used as a vaccine (emphasis added)." Based on the

Applicant: Aoki et al.
Serial No.: 09/845,514
Filed: April 30, 2001
Page 6 of 7

foregoing, Applicant submits that botulinum toxoid is not botulinum toxin, and accordingly, the '110 application fails to disclose or even suggest a composition comprising a combination of botulinum toxins or methods of using such a composition, as recited in the pending claims.

In addition, the Office Action states that claims reciting a combination of botulinum neurotoxin type A and botulinum neurotoxin type E are free from the prior art (including the '907 patent). As indicated above, based on the disclosure in the '110 application, if claims reciting a combination of botulinum toxin type A and botulinum toxin type E are free from the prior art, claims directed to combinations of botulinum toxin types A and B, A and C, A and D, B and C, etc. should also be free from the prior art, including the '907 patent. Thus, Applicant submits that all of the pending claims, that is claims 1-9 and 17-29, are free from the prior art.

In view of the above, Applicant submits that the '907 patent is not prior art to the claimed invention, and that claims 1-4, 6-9, 17-20, and 22-28 are not anticipated by, are unobvious from, and are patentable over the '907 patent under 35 U.S.C. §§ 102 and 103.

Item 6 of the Office Action-Status of the Claims

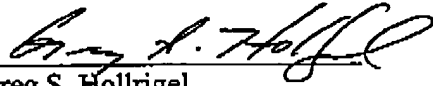
As indicated above, the Office Action states that claims 5, 21, and 29 appear to be free from the prior art, but that these claims are objected to as being dependent upon a rejected base claim. Applicant respectfully submits that claim 29 is not dependent upon a rejected base claim, and therefore, claim 29 should have been indicated to be allowable. In addition, Applicant submits that in view of the foregoing remarks, all of the pending claims, that is claims 1-7 and 17-29 are free from the prior art, and thus, all of the claims should be allowable.

Applicant: Aoki et al.
Serial No.: 09/845,514
Filed: April 30, 2001
Page 7 of 7

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned representative invites the Examiner to telephone him at the number provided below.

Date: 3/13/03

Respectfully submitted,



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MAR-13-03 , 08:05AM FROM-Frank

9494501764

T-184 P.010/012 F-381

EXHIBIT A

1516

• prep. 1 in the direction of. 2 getting nearer to (a goal). 3 in relation to. 4 contributing to the cost

OF *counterparts* (see TO, -WARD).

r • n. a bar fitted to the back of a vehicle, used in a trailer or caravan.

• adj. (of hair) very light blonde.

• n. a piece of thick absorbent cloth or paper used to dry. • v. (towelled, towelling; US *toweled*, *towel*) 1 dry with a towel. 2 (informal, chiefly Austral/NZ) thrash

ME: from OFr *toaille*, of Gmc origin.

ng (US *towelings*) • n. thick absorbent cloth, typically with uncut loops, used for towels and bath-

• n. 1 a tall, narrow building, either free-standing or part of a building such as a church or castle, structure that houses machinery, operators, etc. 3 a structure used as a receptacle or for storage. • v. 1 to reach a great height. 2 (of a bird) soar up to a height, especially (of a falcon) so as to be able to pounce on prey. 3 (as adj, *towering*) very important. 4 (as adj, *towering*) very intense: a *towering*

view *towering* adj. (chiefly positionary) *towary* 20, 21.

OE *torr*; reinforced in ME by OFr *tour*, from L. *torum* Gk.

lock • n. Brit. a tall modern building containing floors of offices or flats.

• n. a tall open-topped structure on a hillside, traditionally placed and leave exposed the someone who has died.

ded • adj. having tow-coloured or untidy hair. 1755 *town-head* n.

/ˈtuː(h)l/, ˈtuː- • n. a North American songbird, usually family, typically secretive in behaviour. [*toil* several species.]

18: imitative of the call of some towhees.

• n. a tow rope. 1 a built-up area with a name, defined boundary, local government, that is larger than a village but smaller than a city. 2 Brit. a chief city of a region. 3 the central part of a neighbourhood, its business or shopping area. 4 densely populated, especially as contrasted with the country or 4 the permanent residents of a university town, contrasted with *comm*. 5 N. Amer. another term for *city* (in sense 3).

go to town informal do something thoroughly or actually on the town informal enjoying the night life or town.

ves *townish* adj. *townlet* n. *townward* 20, 21, 22, 23, 24.

E *town* 'enclosed piece of land, homestead, village' origin.

• n. a limousine.

• n. 1 N. Amer. a public official in charge of the town. 2 (in the UK, until 1974) the secretary or adviser of a town corporation.

ncil • n. (especially in the UK) the elected body in a municipality.

res *town council* n.

r • n. historical a person employed to make public monuments in the streets.

• n. variant spelling of *townsman*.

• n. a dragnet that is towed behind a boat to catch fish.

• n. Brit. chiefly historical coal gas.

• n. a building used for the administration of a town.

se • n. 1 a tall, narrow traditional terrace usually having three or more floors. 2 a modern city house built as one of a row of similar or urban residence of a person owning another in the country. 3 a town hall.

• n. a person who lives in a town.

| i cosy | i: see | d hot | ɔ: saw | ʌ two

1517

town (used especially with reference to their supposed lack of familiarity with rural affairs).

townland • n. (especially in Ireland) a territorial division of land; a township.

town major • n. historical the chief executive officer in a garrison town or fortress.

town mayor • n. Brit. the chairperson of a town council.

town meeting • n. US a meeting of the voters of a town for the transaction of public business.

town planning • n. the planning and control of the construction, growth, and development of a town or other urban area.

- DERIVATIVES *town planner* n.

townscape • n. an urban landscape.

township • n. 1 (in South Africa) a suburb or city of predominantly black occupation, formerly officially designated for black occupation by apartheid legislation. 2 a new area being developed for residential or industrial use by speculators. 3 N. Amer. a division of a county with some corporate powers. 4 a district six miles square. 5 Brit. historical a manor or parish as a territorial division. 6 a small town or village forming part of a large parish. 5 Austral/NZ a small town.

- ORIGIN OE *tūnscipe* 'the inhabitants of a village' (see *town*, -ship).

townsite • n. N. Amer. a tract of land set apart by legal authority to be occupied by a town and usually surveyed and laid out with streets.

townsman (or townswoman) • n. (pl. -men or -women) a person living in a particular town or city. townspeople (also *townsfolk*) • pl. n. the people living in a particular town or city.

towpath • n. a path beside a river or canal, originally used as a pathway for horses towing barges.

towplane • n. an aircraft that tows gliders.

tow rope • n. a rope, cable, etc. used in towing.

toxemia /ˈtɒksɪmiə/ (US *toxemia*) • n. a disease of blood poisoning by toxins from a local bacterial infection. 2 (also *toxæmia* of pregnancy) pro-eclampsia.

- DERIVATIVES *toxæmic* adj.

- ORIGIN C18: from *toxa* + *-emia*.

toxaphene /ˈtɒksəfiːn/ • n. a synthetic amber wax solid with an odour of chlorine and camphor, used as an insecticide.

- ORIGIN 1940s: from *toxa* + (*camphene*, a related terpene).

toxi • comb. form representing *toxic* or *toxin*.

toxic /ˈtɒksɪk/ • adj. poisonous. > of, relating to, or caused by poison. • n. (toxic) poisonous substances.

- DERIVATIVES *toxically* adv. *toxicity* n.

- ORIGIN C17: from med. L. *toxicus* 'poisoned', from L. *toxicon* 'poison'.

toxicant /ˈtɒksɪkənt/ • n. a toxic substance introduced into the environment, e.g. a pesticide.

- ORIGIN C19: var. of *microtoxin*, differentiated in sense.

toxico • comb. form equivalent to *toxic*.

- ORIGIN from Gk *toxikon* 'poison'.

toxicology /ˈtɒksɪkələdʒi/ • n. the branch of science concerned with the nature, effects, and detection of poisons.

- DERIVATIVES *toxicological* adj. *toxicologically* adv. *toxicologist* n.

toxic shock syndrome • n. acute septicæmia in women, typically caused by bacterial infection from a retained tampon or IUD.

toxigenic /ˈtɒksɪdʒənɪk/ • adj. (especially of a bacterium) producing a toxin or toxic effect.

- DERIVATIVES *toxigenicity* n.

toxin /ˈtɒksɪn/ • n. a poison produced by a micro-organism or other organism and acting as an antigen in the body.

- ORIGIN C18: from *toxa* + *-in*.

toxozo • comb. form equivalent to *toxo*.

toxocara /ˈtɒksəˈkærə/ • n. a nematode worm which is a parasite of dogs, cats, and other animals and can be transmitted to humans. (Genus *Toxocara*.)

- DERIVATIVES *toxocarasis* n.

townland | trace

- ORIGIN mod. L., from *toxa* + Gk *kara* 'head'.

toxoid • n. Medicine a chemically modified toxin from a pathogenic micro-organism, which is no longer toxic but is still antigenic and can be used as a vaccine.

toxophilite /ˈtɒksəˈfɪlɪt/ n. • n. a student or lover of archery. • adj. of or relating to archery and archery.

- DERIVATIVES *toxophilist* n.

- ORIGIN C18: from *Toxophilus* (a name invented by the Engl. scholar and writer Roger Ascham, used as the title of his treatise on archery (1545), from Gk *toxos* 'bow' + *-philos* 'loving') + *-ite*.

toxoplasmosis /ˌtɒksəˈplɑːzˈməʊsɪs/ • n. Medicine a disease caused by a parasitic protozoan, transmitted chiefly through undercooked meat, soil, or in cat faeces.

- ORIGIN 1930s: from *Toxoplasma* (genus name) + *-osis*.

toy • n. 1 an object for a child to play with, typically a model or miniature replica of something. > a gadget or machine regarded as providing amusement for an adult. 2 (as modifier) denoting a diminutive breed or variety of dog. • v. (toy with) 1 consider casually or indecisively. > treat (someone) in a superficially amorous way. 2 move or handle absent-mindedly or nervously. > eat or drink in an unenthusiastic or restrained way.

- DERIVATIVES *toylike* adj.

- ORIGIN ME (orig. denoting a funny story or remark): of unknown origin.

toy boy • n. Brit. informal a male lover who is much younger than his partner.

toy-toy /ˈtɔɪˈtɔɪ/ • n. (pl. *toy-toy*) a dance step characterized by high-stepping movements, typically performed at protest gatherings or marches. • n. (*toy-toy*, *toy-toy*, *toy-toy*, *toy-toy*) perform such a dance.

- ORIGIN Ndebele and Shona.

toy town • n. 1 resembling a model of a town in being seemingly in miniature. 2 having no real value or substance.

Tpr • abbrev. Trooper.

TQM • abbrev. Total Quality Management.

TR • abbrev. Turkey (international vehicle registration).

trabeation /ˌtreɪˈbeɪʃ(ə)n/ • n. the use of beams in architectural construction, rather than arches or vaulting.

- DERIVATIVES *trabected* /ˌtreɪˈbedɪd/ adj.

- ORIGIN C18 (denoting a horizontal beam): formed irregularly from L. *trabs*, *trab* 'beam, timber' + *-ation*.

trabecula /ˌtreɪˈbɛkjələ/ • n. (pl. *trabeculae* /-li/) 1 Anat. any each of a series of partitions formed by bands or columns of connective tissue, especially in cancellous bone. 2 Botany a rod-like structure, e.g. a strand of sterile tissue dividing the cavity in a sporangium.

- DERIVATIVES *trabecular* adj. *trabeculate* /-lət/ adj.

- ORIGIN C18: from L., dimin. of *trabs* 'beam, timber'.

tracasseries /ˌtreɪˈkæs(ə)rɪz/ • pl. n. trivial petty quarrels or annoyances.

- ORIGIN Fr., from *tracasser* 'to bustle or fuss'.

trace' • v. 1 find by investigation. > find or describe the origin or development of. 2 follow the course or position of with one's eye, mind, or finger. 3 copy (a drawing, map, or design) by drawing over its lines on a superimposed piece of transparent paper. > draw (a pattern or line). 4 give an outline of. • n. 1 a mark, object, or other indication of the existence or passing of something. > a physical change in the brain associated with a memory. 2 a very small quantity. > a barely discernible indication: a trace of a smile. 3 a line or pattern corresponding to something which is being recorded or measured. > the projection or intersection of a curve on or with a plane. 4 a procedure to trace something, such as the place from which a telephone call was made. 5 Mathematics the sum of the elements in the principal diagonal of a square matrix. 6 W. Indian & N. Amer. a path or track.

- DERIVATIVES *traceability* n. *traceable* adj. *traceless* adj.

- ORIGIN ME: from OFr. *trac* (n.), *tracier* (v.), based on L. *tractus* (see *TRACT*).

trace' • n. each of the two side straps, chains, or ropes by which a horse is attached to a vehicle that it is pulling.

u put | ɪ: too | ʌt my | ʌu how | eɪ day | əu no | ɪə near | ɔɪ boy | ʊə poor | ʌɪr fire | ʌuə sour

The Concise Oxford Dictionary

TENTH EDITION

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Judy Pearsall

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